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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,417	08/14/2002	Rainer H Muller	668-59190	8775

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EXAMINER	
BERKO, RETFORD O	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,417	MULLER ET AL.	
	Examiner	Art Unit	
	Retford Berko	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 22-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 22-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement: The Amendment filed 2/23/03 is acknowledged.

Correction of Record and Status of Claims:

1. At the time of preparing the previous Office Action, only claims 1-27 were posted on E-Dan. These claims were examined and were the subject of the previous Office Action.

2. Claim 21 was canceled by applicant as a result of the amendment.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1-4, 7, 10, 11, 13, 15, 22 and 27 are rejected under 35 USC 102(e) as anticipated by Muller et al (US 5, 858, 410).

Muller et al (Patent '410) teaches a method for preparing nanoparticles of drugs (e.g. corticoids such as prednisolone---see col 22, lin 40-45); the drug particles having average size of 10-1, 000 nanometers by dispersing solid therapeutically active drugs in a solvent and subjecting the dispersion to high pressure homogenization in a piston-gap homogenizer (abstract and col 20, lin 23-30) at room temperature (i.e. under 90 degrees; col 20, lin 35-40).

Claims 1-4, 7, 10, 11, 13, 15, 22 and 27 are anticipated by ' 410.

Claim Rejections - 35 USC § 103

The rejection of claims 1-20 and 22-45 rejected under 35 U.S.C.103(a) as being unpatentable over Desai et al (WO 98/14174).

Desai et al (Patent WO '174) discloses a process for preparation of microparticles or nanoparticles of water insoluble drugs; e.g. paclitazel, an agent that is insoluble in water. The drug is dissolved in an organic solvent (page 17, lin 15-25); a protein such as albumin is added to stabilize the nanoparticles (page 17, lin 31-34) and the mixture is homogenized under high pressure homogenization (page 18, lin 6-15 and page 51, lin 25). In disclosing a method for making a pharmaceutically acceptable formulation, WO '174 discusses sterile-filtration and how drug of particle size less than 200 nm is obtained (page 19, lin 1-16 ; page 10, lin 24 and page 20, lin 30-35). According to Desai, the drug particles can be in crystalline or amorphous for (page 13, lin 5-10): details of how to make drug particles of size less than 200 nm are provided. Furthermore, Desai et al also disclose the effect the solvent used has on drug particle size (page 38, lin 5-20) and further discuss the advantage of making the composition in the form of albumin-paclitazel combination—low toxicity.

One of ordinary skill in the art would be motivated to make paclitazel or itraconazole compositions according to the methods disclosed in the cited prior art wherein the methods have been shown to provide advantages of reduced volumes and low toxicity products. One of ordinary skill would expect to obtain economic advantage of making stable aqueous suspensions of water-insoluble drug such as paclitazel in ready-to-use formulation while maintaining low toxicity of the drug in humans. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made.

Response To Arguments

Applicant's remarks and arguments have been considered but are found unpersuasive:

Applicant argues that Muller's disclosure does not refer to high pressure homogenization, but rather to the milling techniques mentioned in col. 2, lines 56-60, i.e. colloid mills (rotor stator principle), ball or pearl mills. There is no teaching for using these media for high pressure homogenization with piston-gap or jet stream homogenizers, that the reference identify the medium used and that the instant claims are distinguished from Muller et al.

In response, Muller discloses high pressure homogenization (col 20, lin 20-25; col 5, lin 1-5) and identifies various media used in the process including glycerol (Example 4, col 12, lin 30-35) and mannitol (Example 8 at col 14, lin 10-19).

Applicant contends that after dissolution of a drug, preparation of particles by grinding is not possible any more, because after dissolution a solution is present and that Muller's disclosure does not describe dissolution or dispersion of a drug in organic solvents.

In response, contrary to applicant's contention, Muller discloses dispersion of drug in a solvent (claim 38 at col 20, lin 21) and impact dispersion for preparation of nanosuspension of a drug (Example 14 at col 17, lin 15-25).

Applicant argues that the instant invention is novel in that they have found that during homogenization using a piston-gap homogenizer, water vapor can be created in the form of bubbles, which subsequently implode and that the resulting implosion shock waves lead to particle diminution; contending that in such process many materials are destroyed, melted or otherwise undesirably altered by these violent shock waves and that applicants have solved the problem by providing a far more gentler method of obtaining the same particle size without

using the implosion shock waves entailing reducing the temperature (less that 90 degrees) and reducing or eliminating the use of water.

Contrary to applicant's assertion, examiner understands the disclosure in Muller to show that applicant's invention is not novel because Muller disclosed the same piston-gap high pressure homogenization for preparation of drug nanosuspension (col 5, lin 27-34) in organic solvent (abstract) at room temperature (col 20, lin 35-40).

Applicant argues that Desai only discloses an emulsion consisting of nanodroplets results from the high pressure homogenization process, that solvent evaporation is required in order to yield particles of drug and that the process is unlike the instant invention wherein a solid particle suspension is formed and claimed.

ROB

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Retford Berko** whose telephone number is571-272-0590. The examiner can normally be reached on M-F from 8.00 am to 5.30 pm

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Thurman K Page**, can be reached on 571-272-0602.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NEIL S. LEVY
PRIMARY EXAMINER